# Cara Therapeutics Announces No Modifications in Trial Size After Completion of Interim Statistical Assessment For KALM-1 Phase 3 Trial Of KORSUVA™ Injection in Hemodialysis Patients with Pruritus

January 2, 2019

***- Trial continues as planned with enrollment target of 350 patients -***

***- Top-line data readout expected in the first half of 2019 -***

STAMFORD, Conn., Jan. 02, 2019 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors, today announced the completion of an interim statistical analysis of its pivotal KALM-1 Phase 3 trial of KORSUVA™ (CR845/difelikefalin) Injection in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP).

Based on the recommendation of the Independent Data Monitoring Committee (IDMC), the trial will continue as planned with no changes to the original enrollment target of 350 patients. The IDMC's recommendation was based on the results of a prespecified interim conditional power assessment conducted after approximately 50 percent of the targeted patient number completed the designated 12-week treatment period.

"CKD-associated pruritus is a significant unmet need in patients undergoing hemodialysis, with no effective therapies approved in the United States or Europe," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We are very pleased with the IDMC recommendation that the KALM-1 trial proceed as planned with no modifications, and we look forward to completing the study and reporting top-line data in the first half of this year."

**KALM-1 Phase 3 Trial Design**

The Phase 3 U.S. study is a multicenter, randomized, double-blind, placebo-controlled 12-week treatment trial (with a 52-week open label extension phase) that is designed to evaluate the safety and efficacy of 0.5 mcg/kg CR845/difelikefalin injection in 350 hemodialysis patients with moderate-to-severe pruritus.

The primary efficacy endpoint is the proportion of patients achieving at least a 3-point improvement from baseline in the weekly mean of the daily 24-hour worst itching intensity Numeric Rating Scale (NRS) score at week 12. In a completed Phase 2 trial, the proportion of patients with an improvement from baseline in the weekly mean worst itching intensity NRS score of ≥3 points at week 8 was statistically significantly higher in the CR845/difelikefalin 0.5 mcg/kg group compared to the placebo group (64% vs. 29%; p<0.01). [1]

The Phase 3 trial's secondary endpoints include assessment of itch-related quality of life changes measured using the validated self-assessment 5-D itch and Skindex-10 scales, as well as the proportion of patients achieving > 4-point improvement from baseline in weekly mean of the daily 24-hour worst itching NRS score at week 12.

References:

1. Data presentation at 2017 American Society of Nephrology's Annual Meeting (Kidney Week 2017).

**About Cara Therapeutics**
Cara Therapeutics is a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus and pain by selectively targeting peripheral kappa opioid receptors (KORs). Cara is developing a novel and proprietary class of product candidates, led by KORSUVA™ (CR845/difelikefalin), a first-in-class KOR agonist that targets the body's peripheral nervous system, as well as certain immune cells. In Phase 2 trials, KORSUVA Injection has demonstrated statistically significant reductions in itch intensity and concomitant improvement in quality of life measures in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP), and is currently being investigated in Phase 3 trials in hemodialysis patients with CKD-aP. Additionally, in a Phase 2/3 trial in post-operative patients, I.V. CR845/difelikefalin has demonstrated reduction in moderate-to-severe pain, while also reducing the incidence and intensity of nausea and vomiting throughout the post-operative period.

The FDA has conditionally accepted KORSUVA™ as the trade name for difelikefalin injection. CR845/difelikefalin is an investigational drug product and its safety and efficacy have not been fully evaluated by any regulatory authority.

**Forward-looking Statements**
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these forward-looking statements include statements concerning the ongoing trials and future development of the Company's product candidates, including the timing for completion of Cara's KALM-1 Phase 3 clinical trial, or the potential of KORSUVA Injection to be a therapeutic option for hemodialysis patients with CKD-aP. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in Cara's filings with the Securities and Exchange Commission, including the "Risk Factors" section of Cara's Annual Report on Form 10-K for the year ended December 31, 2017 and its other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-

looking statements contained in this press release speak only as of the date on which they were made. Except to the extent required by law, Cara undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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